

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Walter CALLEN et al. Art Unit : 1652
Serial No. : 10/081,739 Examiner : Manjunath N. Rao, Ph.D.
Filed : February 21, 2002
Title : ENZYMES HAVING ALPHA AMYLASE ACTIVITY AND METHODS OF
USE THEREOF

Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, Jay Short, am an expert in the field of molecular biology and enzyme development and was an expert at the time of the invention. I am presently employed as CEO and as a research scientist at Diversa Corporation, San Diego, CA, assignee of the above-referenced patent application. My resume is attached as documentation of my credentials.

2. I declare that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art for screening polypeptides for amylase activity was very high. Procedures for making amylase enzyme fragments and sequence variations, e.g., with substitutions, deletions, insertions, and additions, were routine in the art at the time of the invention. Assays for identifying amylase enzyme fragments were conventional and routine in the art at the time of the invention. Assays for identifying variant polypeptides having amylase activity were conventional and routine in the art at the time of the invention. For example, assays for identifying polypeptides having amylase activity are described in the specification, e.g., on pages 98 to 99 (in Example 5) of the specification, e.g., using FITC-starch in a 384-well plate (page 99, lines 13 to 18). Furthermore, amylase activity assays also were well known in the art at the time of the invention, e.g., as described in USPNs 4,762,917 and 5,319,076 (describing modified oligosaccharide derivatives useful as substrates for measuring amylase activity and activity assays using same); 5,188,956; 5,366,883; 5,370,997; 5,578,479; 5,753,460, to list only a few examples. Many of these assays could have been adapted and used in high-throughput screening assays, which were well known in the art at the time of the invention. Thus, using the teaching of the specification one of ordinary skill in the art would have been able to routinely

make and use the claimed genus of nucleic acids and polypeptides without undue experimentation.

3. I declare that it would not have been necessary for the skilled artisan to understand which regions of the amylases of the invention could be modified to gain or change a function or activity, or be modified without loss of a function or activity. It would not have been necessary for the skilled artisan to understand which specific regions of the amylase sequence or structure needed to be modified without affecting function or activity to routinely generate the genus of nucleic acids and polypeptides of the invention. Screening procedures – including high throughput assays – that could have been used to identify the genus of nucleic acids of the invention, including identifying nucleic acids encoding amylase activity under various conditions, were well known in the art and at the time the application was filed. Methods for making and screening sequence modifications and enzyme fragments were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate amylase-encoding sequences without need of knowing which specific regions of a sequence or structure affected function or activity. Thus, methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (amylase) screening made methods that required previous knowledge of what regions of polypeptide structure could be modified without losing activity obsolete and unnecessary.


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D1530-6US

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date: 5/11/05


Jay Short